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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,311	03/24/2006	Richard F. Ambinder	43369-103949	2676

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
12/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patent-ch@btlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/528,311	AMBINDER ET AL.	
	Examiner	Art Unit	
	BAO LI	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *5-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 10-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment and argument filed on Sept. 12, 2008. Claim 1 has been amended. Clams 1-5 and 9-57 are pending. Claims 1-4 and 10-57 in the scope of the elected species of EBV LMP-2 and GM-CSF are considered. Claims 5-9 were withdrawn from consideration.

Claim Rejections - 35 USC § 101

1. **(withdrawn)** The rejection of claims 1-4 and 10-13 under ***35 USC § 101*** for the non-statutory subject matter issue has been withdrawn necessitated by Applicants' amendment.

Claim Rejections - 35 USC § 112

2. **(withdrawn)** Applicants' argument regarding the rejection of claims 1-4 and 10-57 for the enablement issue related to the deposit requirement has been found persuasive and withdrawn.

3. **(withdrawn)** The rejection f claims 16-57 under 35 U.S.C. 112, first paragraph are moot in view of a new ground rejection upon further considering the pending claims.

New Grounds of Rejections

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (e) as follows:

5. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

6. The disclosure of the prior-filed application, Application No. 60,411,990, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. In particular, the provisional Application only present a human K562 cell line is transformed to express EBV antigen selected from group consisting of EBNA1, LAMP1, LMP2 and GM-CSF However, it does not describe anything related to using said cell line to inducing immune response to treat and prevent any of cancer associated and non-associated with EBV infection. Therefore, the provisional Application lacks the support for the broad scope of claims cited in claims 4, 16-57.

7. Therefore, the priority of claims 4 and 16-57 are only considered to be the effective filling date of PCT/US 03/29684, on Sept. 19, 2003.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 16-57 are rejected under 35 U.S.C. 112, first paragraph for the scope of enablement issue, because the specification, while being enabling for having a K562 cell line transformed with genes expressing GM-CSF and an EBV antigen and using this cell line to stimulate EBV specific T cell activation when it is administered into the patients having EBV associated cancer or EBV infection, does not reasonably provide enablement for using said method to induce a prophylactic immune response to prevent EBV infection or prevent EBV associated cancer development for any person at risk as claims drafted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to male and use the invention commensurate in scope with these claims.

10. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required based upon factors set forth below:

1). The nature of invention, 2). Scope of the claims, 3). State of art and Unpredictability of the field, 4). Working example presented in the specification; 5). Guidance provide in the specification; 6). Level of skill in the art, 7). Amount of the work to fulfill the scope of the claims.

11. The nature of the invention is directed to a method using K562 cell line transformed with EBV antigen and gene encoding GM-CSF to stimulate CD8 T cell response against EBV antigen when it is administered into a patient having EBV associated cancer. The broad scope of the claims reads on a method using said cell line to induce a prophylactic immune response to treat as well as prevent EBV infection or prevent EBV associated cancer development for any person at risk.

12. The state of art teaches that K562 cell line can be transfected with plasmids encoding cytokine GM-CSF and EBV antigen, wherein K562 cell line inherently lacks of MHC-I and MHC-II expression and serves as a universal cell line capable of inducing EBV specific immune response when it is administered into an animal having EBV associated cancer as evidenced by Borrello et al. (Human Gen Therapy, 1999, Vol. 10, pp. 1983-1991). It is also well know in the art that cancers/tumors are caused or developed by many different mechanisms and/or different cancer/tumor related gene expressions as evidenced by Nawrocki et al. (Cancer Treatment Reviews, Vol. 25, No. 1, February 1999, Pages 29-46). Not all cancers /tumors are related to the EBV infection. Therefore, it is unpredictable that the administering the claimed human cell line is able to produce a prophylactic immune response to any or all kinds of cancers or tumors before the person infected with an EBV infection.

13. The specification only presents an example for establishing the K562 cell line transformed to express the EBV antigen EBAV-1 and GM-CSF and a method of using said cell line in patients having EBV associated lymphomas to produce EBV specific T cell immune response. However, the specification lacks sufficient evidence to support the broadly claimed scope of invention directed to using said cell line to prevent EBV infection and EBV associated cancer development.

14. The level of the skill in art for preventing cancer development is very high. Upon considering a large quantity of experimentation needed, the unpredictability of the field, the state

of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-4, 11-12, 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Borrello et al. (Human Gen Therapy, 1999, Vol. 10, pp. 1983-1991).

17. Borrello et al. describe a universal K562 cell line transfected with plasmid encoding cytokine GM-CSF and EBNA-1 of an EBV antigen. Borrello et al. also teach a method using said cell line as a cancer therapeutic composition to induce an immune response against murine melanoma in mice bearing said tumor (See page 185). Therefore, claims 1-2, 11-12 and 14-15 are anticipated by the cited reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 1-4 and 10-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borrello et al. (Human Gen Therapy, 1999, Vol. 10, pp. 1983-1991) and Lee et al. (J. Immunol. 1997, Vol. 158, pp. 3325-3334).

19. The claims invention is drawn to an isolated cell line preferably K562 that lacks MHC-1 and MHCII expression and is transfected to express an immunomodulatory gene of GM-CSF and an gene encoding EBV associated tumor antigen selected from EBNA-1, LMP-1 or LMP-2,

more preferably LPM-2. The invention is also drawn to a method for using same human cell line as immunogenic composition for inducing an immune response against EBV-associated cancer.

20. Borrello et al. describe a universal K562 cell line transfected with plasmid encoding cytokine GM-CSF and EBNA-1 of an EBV antigen. Borrello et al. also teach a method using said cell line as a cancer therapeutic composition to induce an immune response against murine melanoma in mice bearing said tumor (See page 185). Borrello et al. do not teach expressing EBV LMP-2 antigen by K562 cells and extending the in vivo treatment from animal model to human with/without a cancer or tumor, wherein the cancer is Hodkin's lymphoma (HD) and nasopharyngel carcinoma (NPC).

21. Prior to the current Application was filed, the state of art had already taught as evidenced by Lee et al. that EBV is associated with human malignancies of many kinds of lymphomas including HD and NPC. By establishing an EBV specific CTL responses, the EBV-positive lymphoma was clearly disappeared in two clinical studies. They have identified that EBV MLP-2 antigen epitopes capable of inducing a LMP-2-specific CTL response, which can be used effectively for the treatment for HD and NPC (See entire document, especially, pages 3326-3334).

22. Therefore, it would have been obvious for any person ordinarily skilled in the art to combine the teachings by Borrelo et al. and Lee et al. to induce EBV specific CTL response using MPL-2 antigen in DH and NPC patients with an reasonable expectation of success, because both references positively teach that EBV particular antigen ENBV-1 or LMP-2 is an effective CTL antigen capable of inducing an effective CTL immune response against DH or NPC. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BAO LI whose telephone number is (571)272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/
Examiner, Art Unit 1648
11/12/2008.